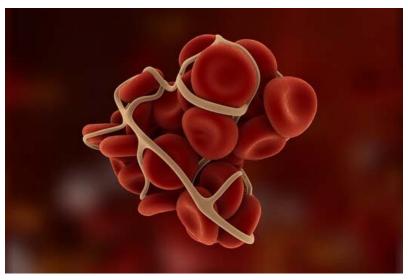
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WEBMD HEALTH NEWS

Blood Clots Are Another Dangerous COVID-19 Mystery



By Brenda Goodman, MA

April 24, 2020 -- Hooman Poor, MD, was tired of watching his patients die, and it looked like another was slipping away.

She was on a ventilator,

Coronavirus Outbreak 2020



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but it wasn't helping. Oxygen wasn't getting to her organs. Acid was building in her blood. Her body was in shock. Her kidneys were failing, but he couldn't put her on dialysis. She was too sick and probably wouldn't survive it.

Poor, a pulmonologist and critical care specialist at Mount Sinai Hospital in New York City, was about to call her family to deliver the crushing news.

As he studied her lab results, he noticed that like many other COVID-19 patients, she had high levels of protein pieces called D-dimers, which are left over when the body breaks up blood clots. Her body was desperately trying, but failing, to clear blood clots, Poor believed.

A Medical Mystery



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Around the world, doctors caring for COVID-19 patients have been trying to make sense of the same thing. When they draw blood from COVID patients, it clots in the tubes. When nurses insert catheters for kidney dialysis and IV lines to draw blood, the tubes quickly become clogged with clots.

"Patients are making clots all over the place," says Adam Cuker, MD, a hematologist and associate professor of medicine at the Hospital of the University of Pennsylvania. "That's making management of these patients very challenging."

Expert Opinion



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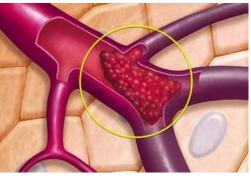
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SLIDESHOW Types of Thrombosis





How Thrombosis1 / 16Starts

Arteries carry blood from your heart to your organs; veins send it back to your heart. Sometimes the smooth flow of blood through these "pipes" slows down or gets blocked. Or, there's damage inside a blood vessel. That's when blood cells can stick together and form a clot. Doctors call this thrombosis. Serious Reviewed by Arefa Cassoobhoy on 4/25/2018

> In addition to the wellknown breathing problems, blood clots are a significant danger for COVID-19 patients. Clots are causing patients with COVID to have heart attacks and strokes; form strange rashes on their skin; and get red, swollen wounds that look like frostbite on their fingers and toes. On autopsy, the small vessels of the lungs and bowels, liver, and

kidneys of COVID patients are choked with clots.

With his patient desperately ill, Poor suspected he had nothing to lose, so he punted.

"This is screaming blood clots. Why don't we try tPA and see if it works?" he said.

He gave his patient a powerful clot-busting drug that's normally used to treat strokes. It's risky. If used improperly, it can cause uncontrolled bleeding, which can be deadly.

Within 30 minutes of getting the drug, his patient showed signs of improvement. Her carbon dioxide levels dropped, and other signs linked to shock seemed to improve. She lived for about another week, before ultimately dying. Poor has tried the drug on other COVID-19 patients, too. It hasn't helped them survive, but he feels like it has shown him something about the disease.

"It did bring to light the possibility that blood clots are playing a bigger role in this disorder than we previously appreciated," he says.

Lessons from the Dead

Sharon Fox, MD, PhD, agrees with him. She's a pathologist at Louisiana State University Health in New Orleans and has been doing autopsies on patients who have died with COVID-19. She's finished 20 cases so far, and they share something in common: They are riddled with blood clots in the smallest vessels of the body. Lungs seem to be especially hard-hit. There, clots appear to have cut off blood flow to the small air sacs where blood cells would be exchanging oxygen and carbon dioxide.

"There's no ability for the blood to flow through and exchange oxygen like it should," she says.

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Though COVID-19 mainly affects the lungs, the virus can make it harder for your heart to function as it should.

(i) ABOUT



Fox says the pattern of damage is striking.

"I've never had a series of cases like this, where they all look the same, and all of the lungs have a similar pattern. There are types of vascular injury at autopsy that I haven't seen before. I would say it's new," she says.

Dangerous blood clotting is always a risk for critically ill patients. That's especially true for those who are immobilized and on mechanical ventilators, as patients with COVID-19 often are. But a recent French study, which compared 150 patients with COVIDrelated respiratory failure who were treated in intensive care units to 145 patients who had respiratory failure, but were not infected with the new coronavirus, found significantly higher rates of blood clotting in the COVID patients.

"We still need more controlled data, but

based on clinical observations and the few studies that have been published, it looks like thrombosis [blood clotting] is more common in these patients," Cuker says.

Why blood congeals the way it does in some COVID patients is still an open question.

One theory is that the body launches an immune attack called a cytokine storm to fight the virus that becomes self-directed, causing cells to kill themselves in an attempt to shut down the infection. Doctors believe that for some patients, the immune attack can end up doing the body more damage than the virus itself. This hyper-inflamed state is itself a well-known risk for blood clots. Cytokine storms can cause a

condition called disseminated intravascular coagulation, or DIC, where patients both bleed uncontrollably and clot too much at the same time.

Another possibility is that the virus may more directly cause the clotting.

New Insights into 'Why'

A research letter published this week in *The Lancet* reported evidence of viral bodies of the new coronavirus invading endothelial cells. The endothelium is the lining of our blood vessels. It directs important functions of the vascular system like clotting and swelling.

Images captured with an electron microscope found traces of the coronavirus in endothelial cells in the heart, kidney, small bowel, and lung -- pretty much all over the body. Researchers collected the tissues during autopsies of three patients who died of COVID-19.

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Study co-author Mandeep Mehra, MD, medical director of the Brigham and Women's Heart and Vascular Center in Boston, says the findings suggest that the virus can directly infect the endothelium. He says that while COVID-19 can certainly cause breathing problems, he doesn't think it's just a lung disease.

"This is actually a disease of the endothelium," he says.

Mehra says the infection starts in the lungs because breathing is the easiest way for the virus to enter the body. Once it infects the lung cells and begins to destroy them, it travels into the bloodstream. There, it infects endothelial cells, causing endotheliitis.

Mehra thinks this endotheliitis comes from not only the direct infection of the blood vessel cells, but also from the haywire cytokine storm that the body launches to fight it off. "We've shown evidence of both."

He says this theory of

infection explains some things that doctors have been trying to puzzle out.

For example, certain conditions like high blood pressure, diabetes, and heart disease stress the endothelium. It's no surprise, then, that people who have these conditions are also the ones who get the sickest when they catch COVID-19.

It also helps to explain why patients have such low oxygen in their blood, but their lungs may not be as stiff as they typically are in patients who have respiratory distress with pneumonia.

Mehra explains that one consequence of endotheliitis is that blood vessels can't constrict the way they normally would. Typically, when a part of the lung becomes damaged, tiny blood vessels in that area close off so that blood will flow to a part of the lung that's still working, where it can collect oxygen. This system protects the body from a sudden drop in oxygen, and it appears to break down in patients with severe COVID-19 infections. Mehra believes the infection of the endothelium is to blame.

The bottom line, he says, is that clotting is a feature of the COVID-19 syndrome. When it becomes a big problem, the disease is advanced and very severe. For that reason, treating the resulting blood clots probably won't work.

He believes something worth trying might be to give patients drugs to support the endothelium, like ACE inhibitors and statins, along with antiinflammatory drugs to tackle the cytokine storm, early in the course of the disease, but more research is needed to know for sure.

If COVID-19 is really an endothelial infection, Mehra thinks that also helps to explain why ventilators aren't helping more patients. A study of 5,700 patients hospitalized with COVID-19 in New York City found that while just 12% needed a ventilator to help them breathe, 88% of those patients died.

"It's not acting like influenza or other bacteria pneumonia where you get inflammation in the lungs and fluid buildup and very stiff lungs. That doesn't seem to be the case, at least early on," Poor says.

"The virus is acting as if its primary target is the endothelium," he says.

That means the clots are just part of a much larger problem, one Poor says doctors don't yet know how to solve.

NEWSLETTER

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WebMD Health News | Reviewed by Neha Pathak, MD on April 24, 2020

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